

WHAT IS CLAIMED IS:

1 1. A method for identifying a ligand for a receptor comprising the
2 steps of:

- 3 a) providing a substrate comprising an adsorbent wherein the
4 receptor is bound to the adsorbent;
5 b) exposing the bound receptor to a sample containing the ligand
6 under conditions to allow binding between the receptor and the ligand; and
7 c) detecting bound ligand by desorption spectrometry.

1 2. A method of detecting a genetic package containing a
2 polynucleotide that encodes a polypeptide agent that specifically binds to a target
3 adsorbent, the method comprising the steps of:

- 4 a) providing a substrate comprising a target adsorbent;
5 b) providing a display library that comprises a plurality of different
6 genetic packages, each different genetic package comprising a polynucleotide that
7 comprises a nucleotide sequence that encodes a polypeptide agent, and each different
8 genetic package having a surface on which the encoded polypeptide agent is displayed;
9 c) exposing the substrate to the display library under elution
10 conditions to allow specific binding between a polypeptide agent and the target adsorbent,
11 whereby a genetic package comprising the polypeptide agent is retained on the substrate;
12 and
13 d) detecting a genetic package retained on the substrate by
14 desorption spectrometry.

1 3. The method of claim 2 wherein the display library is a phage
2 display library.

1 4. The method of claim 2 wherein the step of providing the substrate
2 comprising the target adsorbent comprises the steps of:

- 3 i) providing a substrate comprising an adsorbent, wherein
4 the adsorbent retains a target analyte under an elution condition; and

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5 ii) exposing the adsorbent to the target analyte under the
6 elution condition to allow retention of the target analyte by the adsorbent, whereby the
7 target analyte becomes the target adsorbent.

1 5. The method of claim 2 further comprising the step of (e)
2 sequencing the nucleotide sequence that encodes the polypeptide agent.

1 6. The method of claim 2 further comprising the step of (e) isolating
2 the retained genetic package.

1 7. The method of claim 2 further comprising the step of (e) producing
2 the polypeptide agent.

1 8. The method of claim 2 wherein the substrate comprises (1) an
2 adsorbent that binds an anchoring polypeptide and (2) at least one target genetic package
3 having a surface displaying the anchoring polypeptide and a target adsorbent polypeptide,
4 the target genetic package comprising a polynucleotide that comprises a nucleotide
5 sequence that encodes the target adsorbent, wherein the target genetic package is bound
6 to the adsorbent through the anchoring polypeptide.

1 9. The method of claim 2 wherein the substrate comprises a cell or
2 cell membrane.

1 10. The method of claim 2 wherein the target adsorbent comprises a
2 polypeptide that is differentially expressed between cells of different phenotypes.

1 11. The method of claim 3 wherein the phage is M13.

1 12. The method of claim 4 wherein the target analyte is a target
2 polypeptide and the step of ii) exposing the adsorbent comprises the step of producing the
3 target polypeptide *in situ* on the adsorbent by *in vitro* translation of a polynucleotide
4 encoding the target polypeptide.

1 13. The method of claim 5 wherein the step of sequencing comprises
2 amplifying the polynucleotide sequence *in situ* on the substrate.

1 14. The method of claim 7 wherein the step of producing comprises
2 reproducing the retained genetic package that displays the polypeptide agent.

1 15. The method of claim 7 comprising expressing the polypeptide agent
2 from an expression vector that comprises an expression control sequence operatively
3 linked to the nucleotide sequence encoding the polypeptide agent.

1 16. The method of claim 7 further comprising the step of producing a
2 substrate comprising an adsorbent that comprises the polypeptide agent.

1 17. The method of claim 8 wherein the at least one target genetic
2 package is selected from a target display library screened for genetic packages that bind
3 at least one primary target analyte and wherein the adsorbent comprises the primary
4 target analyte.

1 18. The method of claim 11 wherein the polypeptide agent is a single
2 chain antibody.

1 19. The method of claim 12 wherein the target polypeptide is produced
2 *in situ* by *in vitro* translation of a polynucleotide encoding the target polypeptide.

1 20. The method of claim 14 wherein the step of reproducing is carried
2 out *in situ* on the substrate.

1 21. The method of claim 19 wherein the polynucleotide encoding the
2 target polypeptide is produced *in situ* by *in vitro* transcription.

3 22. A substrate for desorption spectrometry comprising an adsorbent
4 that binds an anchoring polypeptide displayed on a surface of a genetic package, wherein
5 the surface of the genetic package further displays a target polypeptide and wherein the

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6 genetic package comprises a polynucleotide comprising a nucleotide sequence that
7 encodes the target polypeptide.

1 23. The substrate of claim 22 wherein the genetic package is an M13
2 phage.

1 24. The substrate of claim 22 wherein the anchoring polypeptide is a
2 fusion polypeptide with gene III protein and the target polypeptide is a fusion polypeptide
3 with gene VIII protein.

1 25. A substrate comprising an adsorbent that comprises a polypeptide
2 agent that specifically binds to a target analyte, the polypeptide agent identified by the
3 method of claim 33.

1 26. The substrate of claim 25 wherein the polypeptide agent is a single
2 chain antibody.

1 27. A method for detecting translation of a polynucleotide comprising
2 the steps of:

3 a) providing a substrate comprising an adsorbent for use in
4 desorption spectrometry;

5 b) contacting the substrate with the polynucleotide encoding a
6 polypeptide and with agents for *in vitro* translation of the polynucleotide, whereby the
7 polypeptide is produced;

8 c) exposing the substrate to an eluant to allow retention of the
9 polypeptide by the adsorbent; and

10 d) detecting retained polypeptide by desorption spectrometry;
11 whereby detection of the polypeptide provides detection of
12 translation of the polynucleotide.

1 28. A method comprising the steps of:

2 a) exposing a first sample to a primary adsorbent and to an eluant
3 to allow retention of a first analyte by the adsorbent, and detecting the adsorbed analyte

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4 by desorption spectrometry, whereby the retained first analyte becomes a secondary
5 adsorbent;

6 b) exposing a second sample to the secondary adsorbent and to an
7 eluant to allow retention of a second analyte by the secondary adsorbent, and detecting
8 the adsorbed second analyte by desorption spectrometry, whereby the retained second
9 analyte becomes a tertiary adsorbent.

1 29. The method of claim 28 further comprising repeating step (b) at
2 least once for a subsequent sample or samples.

1 ~~Sub By~~ 30. A screening method for determining whether an agent modulates
2 binding between a target analyte and an adsorbent comprising the steps of:

3 a) providing a substrate comprising an adsorbent to which the target
4 analyte binds under an elution condition;

5 b) exposing the substrate to the target analyte and to the agent
6 under the elution condition to allow binding between the target analyte and the adsorbent;

7 c) detecting an amount of binding between the target analyte and
8 the adsorbent by desorption spectrometry; and

9 d) determining whether the measured amount is different than a
10 control amount of binding when the substrate is exposed to the target analyte under the
11 elution condition without the agent;

12 whereby a difference between the measured amount and the control
13 amount indicates that the agent modulates binding.

1 31. The method of claim 30 wherein the adsorbent comprises a ligand
2 that specifically binds the target analyte.

1 32. The method of claim 30 wherein the adsorbent comprises a genetic
2 package having a surface that displays a polypeptide ligand that specifically binds the
3 target analyte.

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1 ~~33.~~ ~~Sub B₅~~ The method of claim 30 for screening a combinatorial library of
2 agents comprising exposing each of a plurality of agents in the library to each of a
3 plurality of the adsorbents.

1 34. The method of claim 31 wherein the ligand is an enzyme and the
2 target analyte is a substrate of, or an inhibitor for, the enzyme, or vice-versa.

1 35. The method of claim 31 wherein the ligand is a hormone and the
2 target analyte is a cell surface receptor or an intracellular receptor of the hormone, or
3 vice-versa.

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